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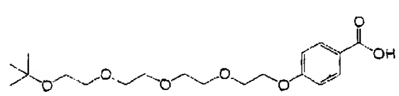

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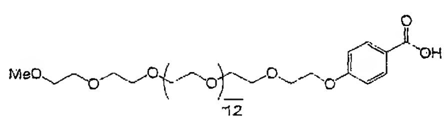

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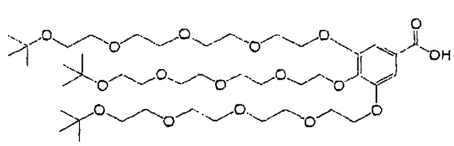

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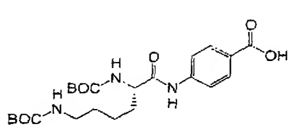

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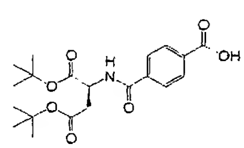

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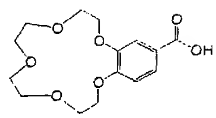

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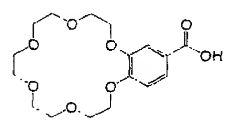

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(57) **Abstract:** The present invention provides for bola amphiphiles compositions which have more than one lyophilic (hydrophilic) head group and a hydrophobic (hydrophobic) moiety capable of hydrogen bonding with other bola amphiphiles. These bola amphiphiles are capable of self assembling into micelles. The advantage of these bola amphiphiles is that they may self-assemble into micelles whose lyophilic head groups are located within the core and on the surface of the micelles. The lyophilic environment at the core and on the surface of the micelles may be different and may be controlled by the choice of head group moieties on the bola amphiphiles. The utility of these compositions is that they can be used to load or encapsulate polar drugs, DNA, mineralizable inorganic salts, or other molecules of interest within the polar interior of the micelle. Such compositions may also provide small water-filled ion-conducting channels within their structure suitable for use in micro electromechanical devices, as templates for nanowires or dielectrics, and as chemical sensors.

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SYNTHESIS AND SELF-ASSEMBLY OF ABC TRIBLOCK BOLA PEPTIDE AMPHIPHILES

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 60/425,536 filed November 12, 2002, entitled **SELF ASSEMBLY OF MULTI-DIMENSIONAL PEPTIDE AMPHIPHILES** and the benefit of U.S. Provisional Application No. 60/425,689 filed November 12, 2002

GOVERNMENT INTEREST

[0002] The United States Government may have certain rights to this invention pursuant to work funded thereby at Northwestern University.

BACKGROUND OF THE INVENTION

[0003] Delivering therapeutic drugs or cell therapies at a controlled release rate to a patient, or delivering encapsulated conductive or magnetic materials at a controlled rate and orientation to process are important goals in medicine and the emerging field of nanotechology manufacturing. Controlling the release of drugs can have a positive effect on therapeutic treatments by maintaining a constant level of the therapy in the patient and also eliminating the need for external intraveneous delivery means or risk of delaying or missing oral administrations of a therapy. Encapsulation can provide enhanced solubility or controlled reactivity for drugs, catalysts, or materials like carbon nanotubes. Micelles and self assembled micelles may allow for the controlled encapsulation and delivery of such materials.

[0004] The functional head groups from the molecules which form the micelle and encapsulate the material should interact favorably with the material to be encapsulated. The formed micelle, including the material, must also have the proper reactivity and solubility for

its intended application. These properties are determined by the head groups on the molecules which are on the exterior of the micelle as well as the intermolecular bonding of the molecules comprising the micelle. For polar drugs, DNA, mineralizable inorganic salts, and other materials with high surface energies, an encapsulating matrix with a polar core is advantageous.

[0005] Bola amphiphiles are molecules in which two or more hydrophilic groups are connected by hydrophobic moieties. Many papers report using peptides as the polar headgroups for symmetrical bola amphiphiles- those in which the head groups are the same. Symmetrical bola-amphiphiles with GlyGly as the hydrophilic headgroups, using saturated hydrocarbon 1,7-heptane dicarboxylic acid have been made (Matsui, H.; Douberly, G.E. *Langmuir* **2001**, *17*, 7918-7922, and 1,12-dodecane dicarboxylic acid in Shimizu, T.; Kogiso, M.; Masuda, M. *J. Am. Chem. Soc.* **1997**, *119*, 6209-6210). A bola-amphiphile with ValVal as a hydrophilic head group for a bola amphiphile was reported by Kogiso, M.; Hanada, T.; Yase, K.; Shimizu, T. *Chem. Comm.* **1998**, *17*, 1791-1792. The dipeptides GlyGly, ProPro, SarSar and (*N*-methyl)Gly(*N*-methyl)Gly and the tripeptides GlyGlyGly, GlyProPro, and GlySarSar are the headgroups in a series of bola amphiphiles with 8-16 carbon hydrocarbon diacids as the hydrophobic spacer as reported in Kogiso, M.; Ohnishi, S.; Yase, K.; Masuda, M.; Shimizu, T. *Langmuir* **1998**, *14*, 4978-4986. The amino acids Ser, Glu, and Asp have also been reported in bola amphiphiles. Asymmetrical bola amphiphile are those amphiphiles where the hydrophilic groups differ in their hydrophilicity. Some examples of asymmetric bola amphiphiles include sugars, and the nucleosides A and T (Shimizu, T.; Iwaura, R.; Masuda, M.; Hanada, T.; Yase, K. *J. Am. Chem. Soc.* **2001**, *123*, 5947-5955). Other examples of asymmetrical bola amphiphiles include those prepared from Lys coupled to 12-amino dodecane carboxylic acid oligomers (Fuhrhop, J.H.; Spiroski, D.; Boettcher, C. *J. Am.*

Chem. Soc. **1993**, *115*, 1600-1601) in which either rods or tubes are obtained. However, these rods do not bury a polar headgroup within the core of the cylindrical micelle.

[0006] There is a need in the art to be able to make self-assembiling micelles from amphiphiles that have lyophilic groups at the core and outer surface of the micelle. It would be further desirable to control the structure, reactivity, and function of such micelles by modification of the amphiphile's molecular structure.

SUMMARY OF THE INVENTION

[0007] The present invention provides for bola amphiphiles compositions which have more than one lyophilic (hydrophilic) head group and a lyophobic (hydrophobic) moiety capable of hydrogen bonding with other bola amphiphiles. These bola amphiphiles are capable of self assembling into micelles. The advantage of these bola amphiphiles is that they may self-assemble into micelles whose lyophilic head groups are located within the core and on the surface of the micelles. The lyophilic environment at the core and on the surface of the micelles may be different and may be controlled by the choice of head group moieties on the bola amphiphiles. The utility of these compositions is that they can be used to load or encapsulate polar drugs, DNA, mineralizable inorganic salts, or other molecules of interest within the polar interior of the micelle. Such compositions may also provide small water-filled ion-conducting channels within their structure suitable for use in micro electromechanical devices, as templates for nanowires or dielectrics, and as chemical sensors.

BRIEF DESCRIPTION OF THE FIGURES

[0008] Various aspects and applications of the present invention will become apparent to the skilled artisan upon consideration of the brief description of the figures and the detailed description of the invention, which follows:

Figure 1 is an illustration of the chemical structure of Bola peptide-amphiphiles, **1-5**, containing single oligo(ethylene glycol) chains;

Figure 2 is an illustration of the chemical structure of Bola peptide-amphiphiles, **6** and **7**, containing multiple or cyclic oligo(ethylene glycol) chains;

Figure 3 is an illustration of the chemical structure of Bola peptide-amphiphiles, **8** and **9**, containing hydroxyls from L-Serine;

Figure 4 is an illustration of the chemical structure of Bola peptide-amphiphiles, **10-13**, with charged headgroups from amino or acid group at both termini;

Figure 5 is an illustration of the chemical building blocks, **14-20**, for Bola peptide-amphiphiles;

Figure 6 is an illustration of synthsis of terminal tetraethylene glycol acid **14**;

Figure 7 is an illustration of the synthesis of the terminal building blocks **15** and **16**;

Figure 8 is an illustration of the synthesis of the terminal building blocks **17** and **18**;

Figure 9 is a TEM image of **2** without staining;

Figure 10 is a TEM image of **2** negatively stained with phosphotungstic acid;

Figure 11 is a TEM image of **2** positively stained with uranyl acetate;

Figure 12 is a TEM image of **4** negatively stained with phosphotungstic acid;

Figure 13 is a TEM image of **6** negatively stained with phosphotungstic acid;

Figure 14 is a TEM image of **7** negatively stained with phosphotungstic acid.

DESCRIPTION OF THE INVENTION

[0009] Cylindrical micelles or nanofibers comprised of self assembled peptide amphiphiles having a hydrophobic core and a hydrophilic shell have been made. The general concept of peptide-amphiphiles that self-assemble into cylindrical micelles have been reviewed in two articles: Hartgerink, J.D., Beniash, E., and Stupp, S.I. *Science* **2001**, 294

(5547) 1684-1688 and Hartgerink, J.D., Beniash, E., and Stupp, S.I. *Proc. Nat. Acad. Sci.* **2002**, 99 (8), 5133-5138, and are incorporated herein by reference in their entirety.

[0010] The addition of a second polar head group to an existing peptide amphiphile or peptide rod amphiphile would form a bola amphiphile and give a triblock structure to these molecules. These molecules would be characterized by two hydrophilic or lyophilic regions, which could be similar or dissimilar from one another, that sandwich a relatively hydrophobic or lyophobic section of the molecule. The lyophobic section of the bola amphiphile molecule is designed to have moieties or functional groups capable of intramolecular hydrogen bonding.

[0011] A bola amphiphile with a tri block structure may self assemble in aqueous solutions into a micelle where the lyophobic portion of the bola amphiphile is excluded from the aqueous solution and the lyophobic groups are directed to the core and surface of the micelle. In traditional aqueous self assembled peptide amphiphiles the lyophobic group is located at the core of the micelle.

[0012] The bola amphiphiles of the present invention create a new lyophilic, rather than lyophobic, core for self assembled micelles that are formed from them. One of the key advantages of such bola amphiphiles and micelle structures over existing bola-amphiphiles would be the presence of hydrogen bonding in the lyophobic region. This stabilizes the self-assembled structure, but also allows for changes in hydrogen-bonding patterns within the lyophobic region of the bola amphiphiles and micelles. This hydrogen bonding can be engineered to encourage a polar arrangement of adjacent molecules, and it may allow for control ot the structure, reactivity, and hence function of the such micelles. A second advantage of these micelles may be that the lyophilic core provides functional groups for transporting ions along the core of the micelle. A water filled ion-conducting channel may function as a sensor. Self assembled bola amphipiles of this type may permit loading or

encapsulation of polar drugs, bioactive peptides, DNA, mineralizable inorganic salts, or other molecules of interest within the polar interior of the micelles or nanofibers.

[0013] One object of the present invention is to provide for a bola amphiphile composition with a lyophobic moiety capable of hydrogen bonding and having a first end and a second end. The first end of the lyophobic moiety is chemically coupled to a first lyophilic head group moiety, and the second end of the lyophobic moiety is chemically coupled bonded to a second lyophilic head group. The molecule formed by the coupling of these groups is a bola amphiphile with a triblock structure. In such a bola amphiphile, the first and second lyophilic heads groups or moieties may have the same or different lyophophilicity. The lyophilic head groups may be peptides, and in a preferred embodiment the amino acids comprising the peptide have at least three non-peptide bond forming amine or acid moieties.

[0014] Other lyophilic head groups for the bola amphiphiles useful in the practice of this invention may be one or more oligo(ethylene glycol) chains, cyclic oligo(ethylene glycols), hydroxyl functionalities from amino acids such as those derived from L-serine, and potentially charged amino or carboxylic acid groups derived from Asp, Lys, 4'-amino-4-biphenyl carboxylic acid, p-amino benzoic acid, 6-aminohexanoic acid. The terminal building blocks **14-18**, and crown ethers such as **19** and **20**,shown in Figure 5, are also useful in the practice of this invention.

[0015] The lyophobic group of the bola amphiphiles has functional groups capable of hydrogen bonding. Examples of groups which may be incorporated into the lyophibic portion of the bola amphiphile include but are not limited to p-amino benzoic acid, p-hydroxy benzoic acid, 4'-amino-biphenyl-4-carboxylic acid, cholesterol, and 6-amino-hexanoic acid. Lyophobic moieties in the bola amphiphile may also be comprised of alkenes, acetylenes, aromatics, and heteroaromatic moieties containing amine, acidic, and hydroxyl functionalities capable of hydrogen bonding. The degree of hydrogen bonding in the lyophobic portion of

the bola amphiphile may be controlled by the number and types of groups chosen to make up the lyophobic group. For example, substitution of 7-amino-hexanoic acid for one or more of the 6-amino-hexanoic acid molecules in **5** would be expected to change the hydrogen bonding due to the greater aliphatic content of the 7-amino-hexanoic acid.

[0016] Another object of this invention is a composition that is a self assembled micelle comprising at least one bola amphiphile. Self assembled micelles can form in a variety of shapes including but not limited to spheres, cylinders, tubes, or disks. Micelles may be formed in water or aqueous solutions containing dissolved salts or other solvents like ethanol. In a preferred embodiment the bola amphiphiles forming the micelle have a lyophobic moiety capable of intermolecular hydrogen bonding with, for example, other lyophobic moieties from bola amphiphiles adjacent to it in a micelle. Lyophilic groups in the bola amphiphile are chemically coupled to opposite ends of the lyophobic moietie. Molecules **1-13** are examples of bola amphiphiles useful in the self assembly of micelles and in the practice of this invention. The lyophilic head groups of the bola amphiphiles which self assemble to form the micelle may be the same or different. In a self assembled solid packed micelle, one of the lyophilic head groups of the bola amphiphile is at the center of the micelle and the other lyophilic head group is oriented toward the outer surface of the micelle. The core and surface of the micelle are substantially lyophilic.

[0017] In a preferred embodiment of this invention, the self assembled micelles form with the lyophilic group of the bola amphiphile at the center of the micelle. In a more preferred embodiment, the self assembled micelles form the weakest lyophilic group of the bola amphiphile at the center of the micelle.

[0018] The bola amphiphile may be prepared as a solution my dissolving it in a suitable solvent. It may then be mixed with materials or therapies for encapsulation. Examples of therapies include pharmaceuticals, chemotherapeutics, immunosuppresents,

anifungals, antibacterials, growth factors, vaccines, tissue/cell culture factors, and antibiotics. Examples of suitable materials include carbon nanotubes, colloidal metals, polymers, magnetic colloids, and semiconductors.

[0019] A method of making a self assembled micelle from bola amphiphile with a lyophobic moiety capable of hydrogen bonding includes the step of making a first solution of a suitable bola-amphiphile in a charged ionic form, mixing the first solution with a second composition which changes the pH of the first solution towards a neutral pH, and reacting the first solution and second compostion until a gel forms. The second composition may be in the form of a solid, liquid, or gas. For example, basic solutions of carboxylate salt based bola amphiphiles gel in water when the pH is lowered, for example, by introduction of HCl vapor. Ammonium salt based bola amphiphiles gel in water when the pH is raised, for example, by exposure of the solution to ammonia vapor. Preferably the bola amphiphile has a lyophobic group capable of hydrogen bonding and the micelle formed has a lyophilic group at the center of the micelle.

[0020] It is another object of this invention to provide for a method of encapsulating a therapeutic treatment in formed by these bola amphiphiles. Preferrably at least one therapeutic agent is mixed with a solution containing a bola amphiphile. This solution is gelled, or self assembled, into micelles of the bola amphiphile with the therapeutic treatment by raising or lower the pH of the solution. Preferably the bola amphiphile has a lyophobic group capable of hydrogen bonding and the micelle formed has a lyophilic group at the center of the micelle.

[0021] It is another object of this invention to provide for a method of treating a patient with a therapeutic agent encapsulated in a self assembled bola amphiphile. The method includes the steps of identifying a site in need of treatment on a patient, and then administering an effective amount of the therapeutic agent encapsulated in the self assembled

bola amphiphile micelles to the site. The micelle encapsulated therapy may be mixed with suitable carriers, made into pills, or mixed with other solutions for administering to the patient.

[0022] It is another object of this invention to provide for a method of encapsulating a carbon nanotube in a bola amphiphile. The method includes mixing carbon nanotubes with a solution of a bola amphiphile capable of self assembly. This mixture is gelled, or self assembled, into micelles of the bola amphiphile with the carbon nanotubes by raising or lower the pH of the solution. Preferably the bola amphiphile has a lyophobic group capable of hydrogen bonding and the micelle formed has a lyophilic group at the center of the micelle.

[0023] The bola PA's are prepared by solid-phase peptide synthetic techniques, using the Fmoc strategy from Rink, preloaded Wang, or preloaded HMPB resins. The bola amphiphiles presented in this disclosure are all of the unsymmetrical variety, although symmetrical ones can be prepared in a similar manner. The exterior headgroups are designed to have three to four amino or carboxylic acid charges, and the interior headgroups are designed to have one oligo(ethylene glycol) chain (**1-5** in Figure 1), multiple or cyclic oligo(ethylene glycol) chains (**6** and **7** in Figure 2), hydroxyl functionalities derived from L-serine (**8** and **9** in Figure 3), and the potentially charged amino or carboxylic acid groups derived from Asp, Lys (K), or 4'-amino-4-biphenyl carboxylic acid (**10-13** in Figure 4). The amino acid residues used in these bola PA's are naturally occurring and commercially available with the exception of *p*-aminobenzoic acid (PABA), used as an Fmoc-beta-Ala-PABA-COOH dimer reported in a previous disclosure, 6-aminohexanoic acid, and the terminal building blocks **14-20** outlined in Figure 5. The solution phase syntheses of the terminal building blocks **14-18** are described in Figures 6-8, and crown ethers **19** and **20** are commercially available.

[0024] The bola PA's can be gelled in the same manner previously described for the original PA's and the peptide rod amphiphiles. The bola PA's with exterior polar amino acid headgroups of KKK or second generation Lys dendrons are cleaved from the resin as their TFA salts and are freely soluble in water, with the exception of insoluble **10**, and are gelled by exposing a 0.2-1.5% by wt solution in water to ammonia vapors. The bola PA's with exterior headgroups of EEE (E = Glu) and EEEG (G = Gly) are charged as their potassium carboxylates by dissolving them in 0.1 N KOH solution at concentrations of 0.2-1.5% by wt, and are gelled by exposure to HCl vapors. Table 1 qualitatively outlines the results of the gelation experiments under these conditions.

[0025] Table 1. Gelation of the Bola PA's by change in pH.

Bola PA	wt %	gelation behavior	clarity
1	1.0	self-supporting gel	clear
	0.77	self-supporting gel	clear
2	1.0	self-supporting gel	opaque/cloudy
	0.5	self-supporting gel	opaque/cloudy
3	1.0	weak gel	opaque
	0.5	weak gel	cloudy
4	1.0	self-supporting gel	clear
	0.5	self-supporting gel	clear
	0.25	self-supporting gel	clear
5	1.0	weak gel	cloudy
	0.5	weak gel pellet	cloudy
	0.25	precipitates	cloudy
6	1.5	self-supporting gel	opaque/cloudy
	1.0	self-supporting gel	opaque/cloudy
	0.5	fragile gel	cloudy
	0.25	precipitates	cloudy
7	1.0	self-supporting gel	cloudy
	0.5	self-supporting gel	cloudy
	0.25	fragile gel	cloudy
8	1.0	fragile gel	cloudy
	0.5	viscous solution	clear
9	1.0	self-supporting gel	clear
	0.5	self-supporting gel	clear
	0.25	self-supporting gel	clear
11	1.0	precipitates	cloudy
	0.5	precipitates	cloudy
12	1.0	self-supporting gel	slightly cloudy
	0.3	self-supporting gel	clear
13	1.0	self-supporting gel	slightly cloudy
	0.5	self-supporting gel	clear
	0.25	self-supporting gel	clear

[0026] The structures of the 1.0% by wt gels of bola PA's **2**, **4**, **6**, and **7** were investigated by TEM. The single tetraethylene glycol chains at the core with EEEG and KKK amino acid sequences at the periphery, in **2** and **4**, respectively, show predominantly nanofiber-like structures of roughly twice the calculated length of the bola PA. Bola PA **2** is shown in Figures 9, 10, and 11 without staining, with negative staining, and with positive staining, respectively. (At this time the data does not absolutely exclude a flat ribbon structure.) The TEM image of **4** negatively stained with phosphotungstic acid is shown in Figure 12. Positive staining with uranyl acetate, as in Figure 11, demonstrates the polar arrangement of ethylene glycol chains at the core and carboxylic acid functionalities at the periphery of the fibers, with the carboxylic acids preferentially stained. Unlike **2** and **4** with a single tetraethylene glycol chain, the negatively stained TEM images of **6** with three chains and **7** with a crown ether in Figures 13 and 14, repectively, show less defined fiber structure. Spherical micelles are observed in Figure 14, in addition to the one-dimensional fiber-like structures. The use of the more crowded ethylene glcyol polar headgroups in **6** and **7** appears to disrupt the cylindrical micelle structure, so that the peptide region would need to be redesigned with a larger cross-sectional area if these headgroups are to be accommodated at the core.

[0027] Uses for the self assembled bola amphiphiles include but are not limited to encapsulation and delivery of therapeutics, tissue engineering, formation of ion channels for sensors and cell therapies, formation of nanowires, and pH responsive cylindrical micelles for the release of micelle-encapsulated materials and the capture of material dissolved in the solution.

[0028] The advantage of these materials is that they self-assemble into cylindrical micelles whose hydrophilic environments, both within the core of the cylinder and at its

periphery, are different and can be controlled by the choice of amino acids or functionalized acid moieties on the bola amphiphiles.

[0029] Although the present invention has been described in considerable detail with reference to certain preferred versions thereof, other versions are possible. For example, …., Therefore, the spirit and scope of the appended claims should not be limited to the description of the preferred versions contained herein.

CLAIMS

What is claimed:

1. A bola amphiphile composition comprising: a lyophobic moiety capable of hydrogen bonding and having a first end and a second end; the first end of said lyophobic moiety chemically coupled to a first lyophilic head group; and the second end of said lyophobic moiety chemically coupled to a second lyophilic head group.

2. The bola amphiphile of claim 1 wherein the first and second lyophilic heads groups are the same.

3. The bola amphiphile as in claim 1 or 2, wherein said lyophilic head groups are peptides.

4. The composition of claim 3 wherein the amino acids comprising the peptide have at least three non-peptide bond forming amine or acid moieties.

5. The bola amphiphile as in claim 1 or 2, wherein said lyophilic head groups are chosen from the group consisting of: oligo(ethylene glycol) chains, cyclic oligo(ethylene glycols), hydroxyl functionalities, amino or carboxylic acid groups, 4'-amino-4-biphenyl carboxylic acids, naturally occurring amino acids, and aminobenzoic acids.

6. A self assembled micelle comprising: at least one bola amphiphile, said bola amphiphile having a lyophobic moiety capable of hydrogen bonding and having a first end

and a second end; the first end of said lyophobic moiety chemically coupled to a first lyophilic head group; and the second end of said lyophobic moiety chemically coupled to a second lyophilic head group.

7. The micelle of claim 6 wherein the lyophilic head groups of the bola amphiphile are different.

8. The micelle of claim 6 wherein the core of the micelle is lyophilic.

9. The micelle of claim 6 wherein the one or more bola amphiphiles comprising the micelle are capable of hydrogen bonding.

10. A self assembled solid packed micelle comprising: at least one bola amphiphile in which one of the lyophilic head groups of the bola amphiphile is at the center of the micelle.

11. The micelle as in claim 10, further comprising a composition chosen from the group consisting of: pharmaceuticals, chemotherapeutics, immunosuppresents, antifungals, antibacterials, growth factors, vaccines, tissue/cell culture factors, and antibiotics.

12. The micelle as in claim 10, further comprising a material chosen from the consisting of: carbon nanotubes, colloidal metals, conductive polymers, magnetic colloids, and semiconductors.

13. A method of making a self assembled micelle from bola amphiphile with a lyophobic moiety capable of hydrogen bonding comprising the step of: making a first solution of a suitable bola-amphiphile in a charged ionic form; mixing the first solution with a second composition which changes the pH of the first solution towards a neutral pH; and reacting the first and second solutions until a gel forms.

14. A method encapsulating a therapeutic treatment comprising: providing a therapeutic agent; exposing said therapeutic to a bola amphiphile capable of self assembly; and initiating self assembly.

15. A method of treating a patient with a therapeutic agent encapsulated in a self assembled bola amphiphile comprising: identifying a site on a patient in need of a treatment; and administering and effective amount of the bola amphiphile encapsulated therapeutic agent to said site in need thereof.

16. A method of encapsulating a nanotube comprising: forming a nanotube; exposing said nanotube to a bola amphiphile capable of self assembly, and initiating self assembly of said bola amphiphile.

17. A bola amphiphile composition comprising: a hydrophobic moiety capable of hydrogen bonding and having a first end and a second end; the first end of said hydrophobic moiety chemically coupled to a first hydrophilic head group; and the second end of said hydrophobic moiety chemically coupled to a second hydrophilic head group.

18. The bola amphiphile of claim 17 wherein the first and second hydrophilic heads groups are the same.

19. The bola amphiphile as in claim 17 or 18, wherein said hydrophilic head groups are peptides.

20. The composition of claim 19 wherein the amino acids comprising the peptide have at least three non-peptide bond forming amine or acid moieties.

21. The bola amphiphile as in claim 17 or 18, wherein said hydrophilic head groups are chosen from the group consisting of: oligo(ethylene glycol) chains, cyclic oligo(ethylene glycols), hydroxyl functionalities, amino or carboxylic acid groups, 4'-amino-4-biphenyl carboxylic acids, naturally occurring amino acids, and aminobenzoic acids.

22. A self assembled micelle comprising: at least one bola amphiphile, said bola amphiphile having a hydrophobic moiety capable of hydrogen bonding and having a first end and a second end; the first end of said hydrophobic moiety chemically coupled to a first

hydrophilic head group; and the second end of said hydrophobic moiety chemically coupled to a second hydrophilic head group.

23. The micelle of claim 22 wherein the hydrophilic head groups of the bola amphiphile are different.

24. The micelle of claim 22 wherein the core of the micelle is hydrophilic.

25. The micelle of claim 22 wherein the one or more bola amphiphiles comprising the micelle are capable of hydrogen bonding.

26. A self assembled solid packed micelle comprising: at least one bola amphiphile in which one of the hydrophilic head groups of the bola amphiphile is at the center of the micelle.

27. The micelle as in claim 26, further comprising a composition chosen from the group consisting of: pharmaceuticals, chemotherapeutics, immunosuppresents, anifungals, antibacterials, growth factors, vaccines, tissue/cell culture factors, and antibiotics.

28. The micelle as in claim 26, further comprising a material chosen from the consisting of: carbon nanotubes, colloidal metals, conductive polymers, magnetic colloids, and semiconductors.

29. A method of making a self assembled micelle from bola amphiphile with a hydrophobic moiety capable of hydrogen bonding comprising the step of: making a first solution of a suitable bola-amphiphile in a charged ionic form; mixing the first solution with a second composition which changes the pH of the first solution towards a neutral pH; and reacting the first and second solutions until a gel forms.

30. A method encapsulating a therapeutic treatment comprising: providing a therapeutic agent; exposing said therapeutic to a bola amphiphile capable of self assembly; and initiating self assembly.

31. A method of treating a patient with a therapeutic agent encapsulated in a self assembled bola amphiphile comprising: identifying a site on a patient in need of a treatment; and administering and effective amount of the bola amphiphile encapsulated therapeutic agent to said site in need thereof.

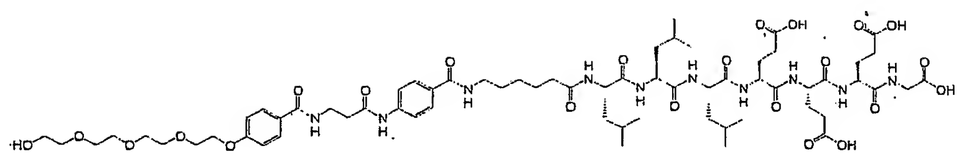
32. A method of encapsulating a nanotube comprising: forming a nanotube; exposing said nanotube to a bola amphiphile capable of self assembly, and initiating self assembly of said bola amphiphile.

33. The micelle as in claim 6, further comprising a composition chosen from the group consisting of: pharmaceuticals, chemotherapeutics, immunosuppresents, antifungals, antibacterials, growth factors, vaccines, tissue/cell culture factors, and antibiotics.

34. The micelle as in claim 6 , further comprising a material chosen from the consisting of: carbon nanotubes, colloidal metals, conductive polymers, magnetic colloids, and semiconductors.

35. The micelle as in claim 22, further comprising a composition chosen from the group consisting of: pharmaceuticals, chemotherapeutics, immunosuppresents, anifungals, antibacterials, growth factors, vaccines, tissue/cell culture factors, and antibiotics.

36. The micelle as in claim 22, further comprising a material chosen from the consisting of: carbon nanotubes, colloidal metals, conductive polymers, magnetic colloids, and semiconductors.



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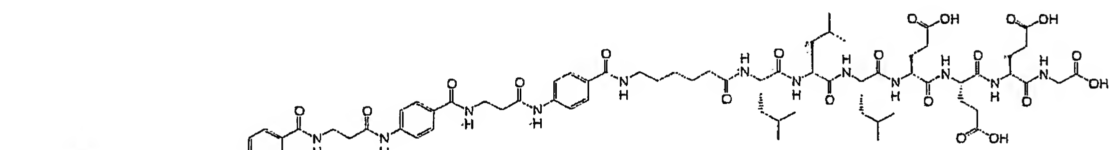

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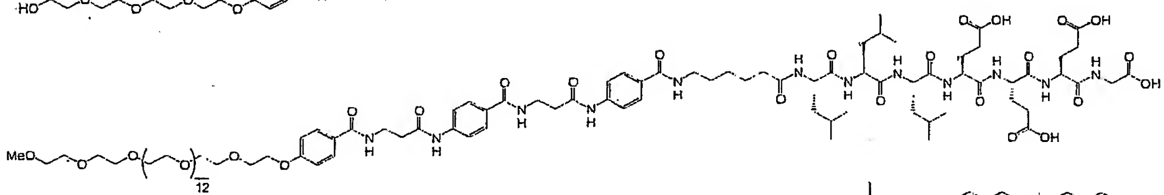

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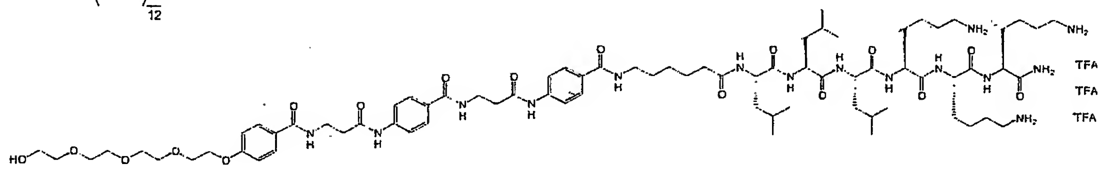

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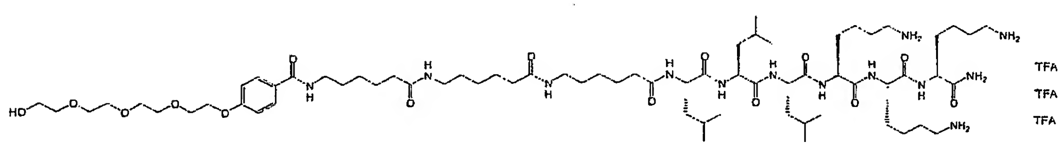

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FIGURE 1

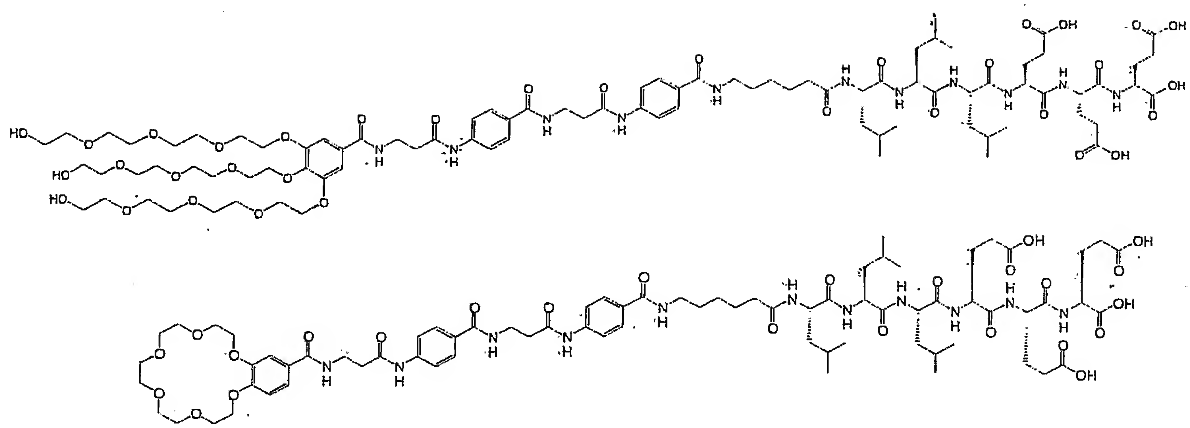


FIGURE 2

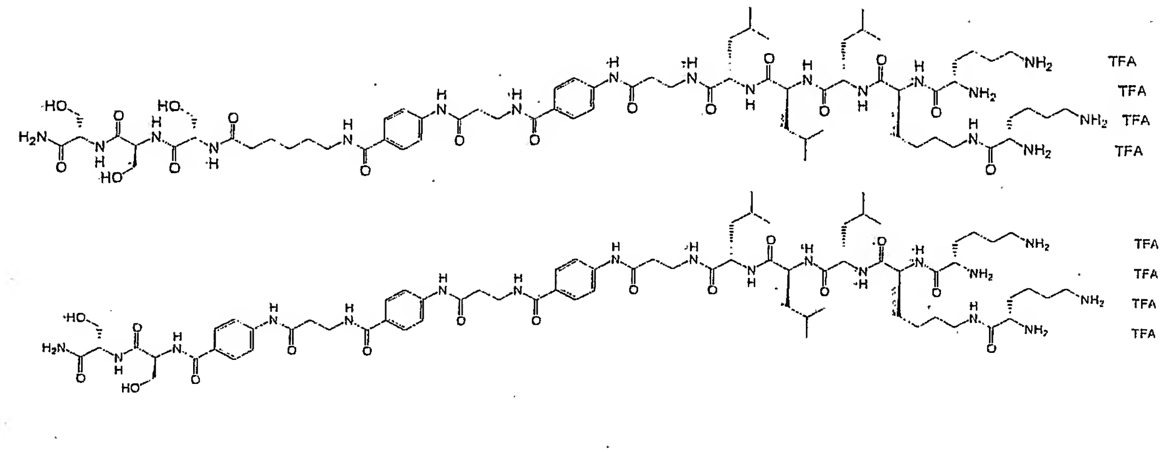
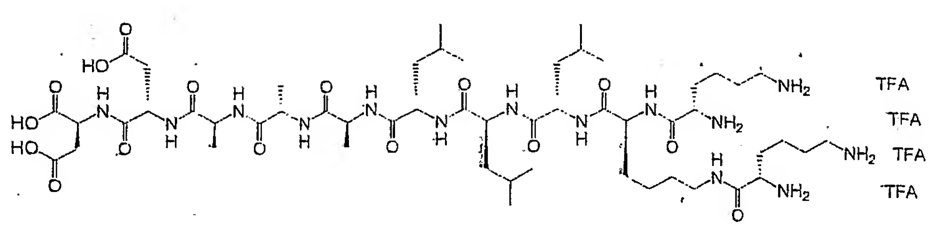


FIGURE 3



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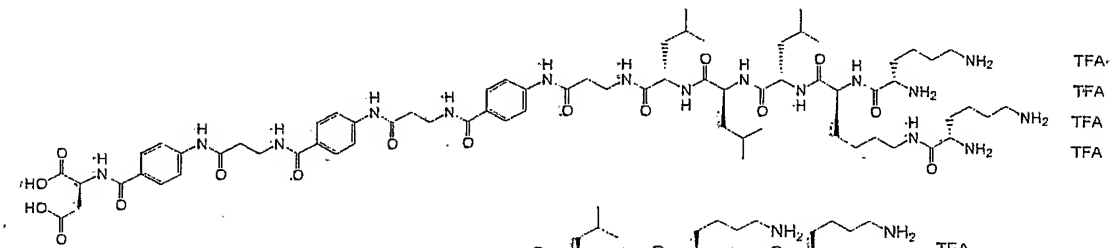

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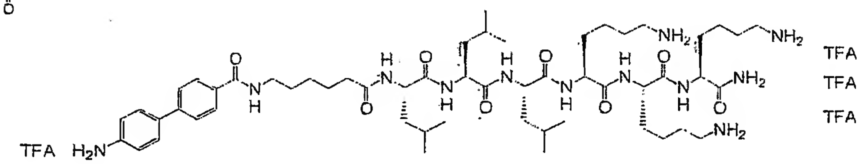

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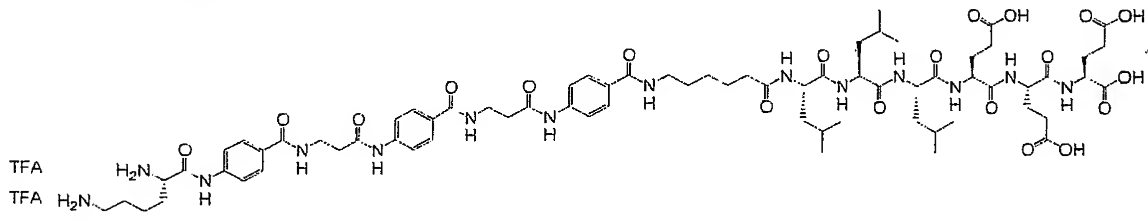

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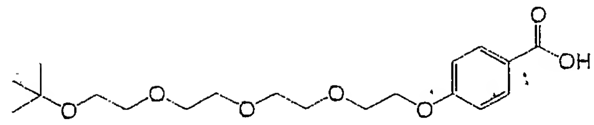
FIGURE 4



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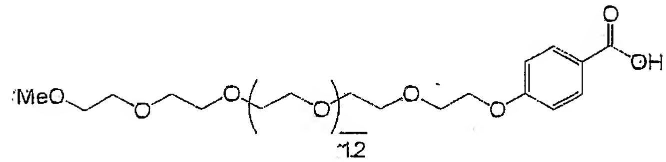

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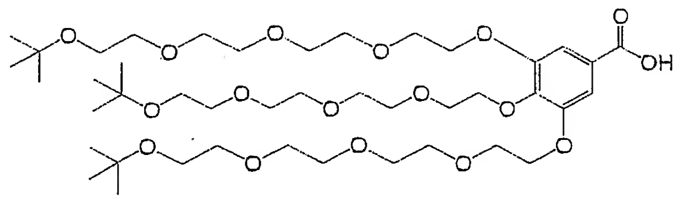

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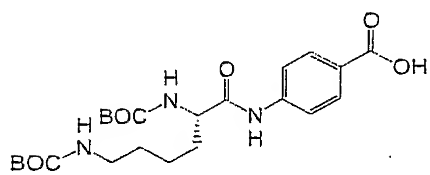

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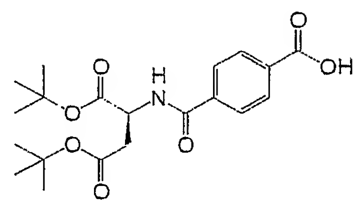

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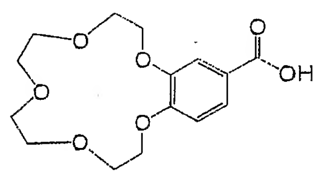

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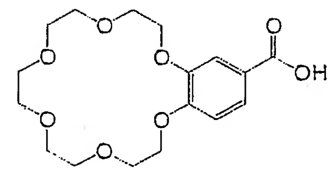

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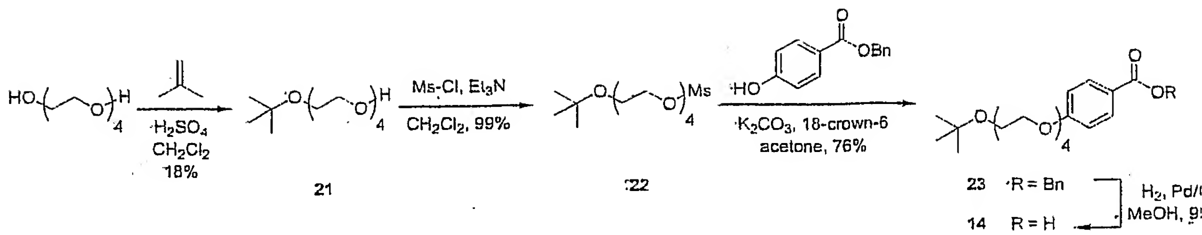
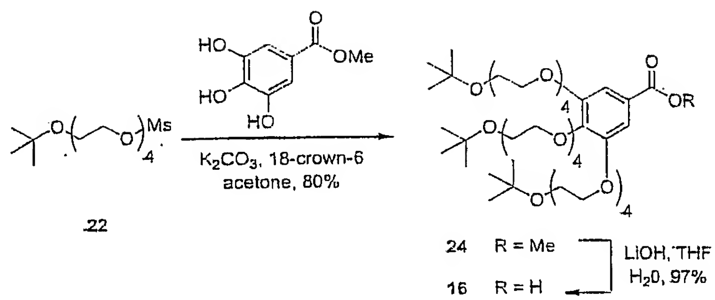
FIGURE 5 - 5/14



HO
H
4
H_2SO_4
CH_2Cl_2
18%
O
H
4
21
Ms-Cl, Et_3N
CH_2Cl_2, 99%
O
Ms
4
22
O
OBn
HO
K_2CO_3, 18-crown-6
acetone, 76%
O
OR
4
23 R = Bn
14 R = H
H_2, Pd/
MeOH, 9

FIGURE 6


HO
HO
HO
O
OMe
O
Ms
4
K2CO3, 18-crown-6
acetone, 80%
22
O
OR
24 R = Me
16 R = H
LiOH, THF
H20, 97%

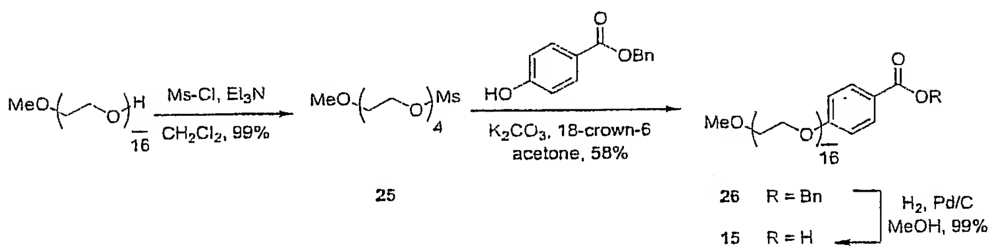

MeO
H
16
Ms-Cl, Et3N
CH2Cl2, 99%
MeO
Ms
4
25
HO
OBn
K2CO3, 18-crown-6
acetone, 58%
MeO
16
OR
26 R = Bn
15 R = H
H2, Pd/C
MeOH, 99%

FIGURE 7

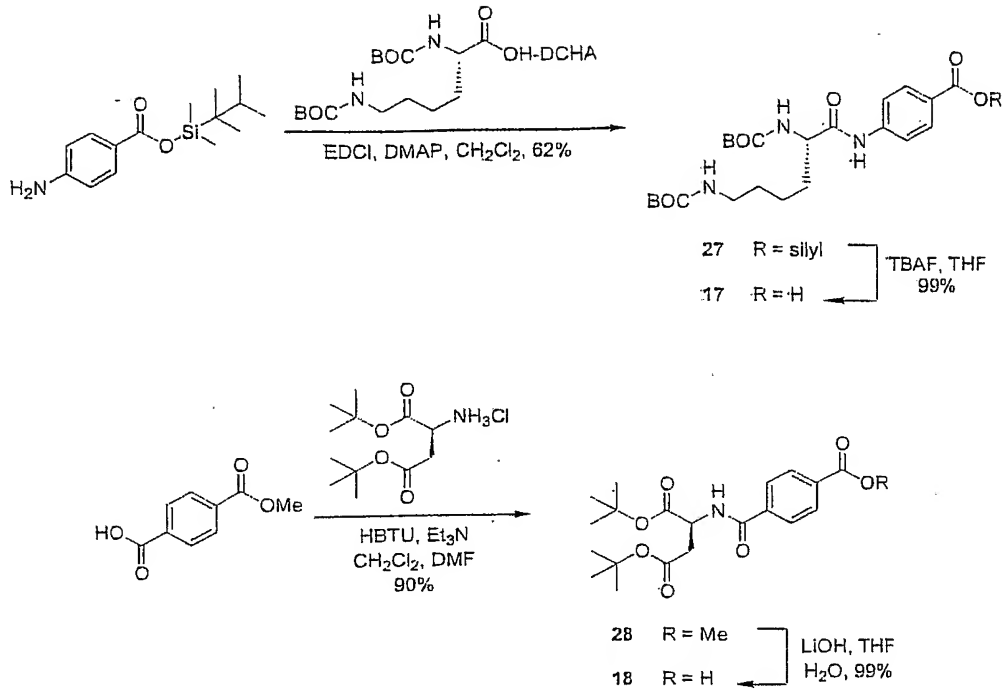

BOC
OH-DCHA
EDCI, DMAP, CH_2Cl_2, 62%
H_2N
OR
27 R = silyl
17 R = H
TBAF, THF
99%
NH_3Cl
OMe
HO
HBTU, Et_3N
CH_2Cl_2, DMF
90%
28 R = Me
18 R = H
LiOH, THF
H_2O, 99%

FIGURE 8

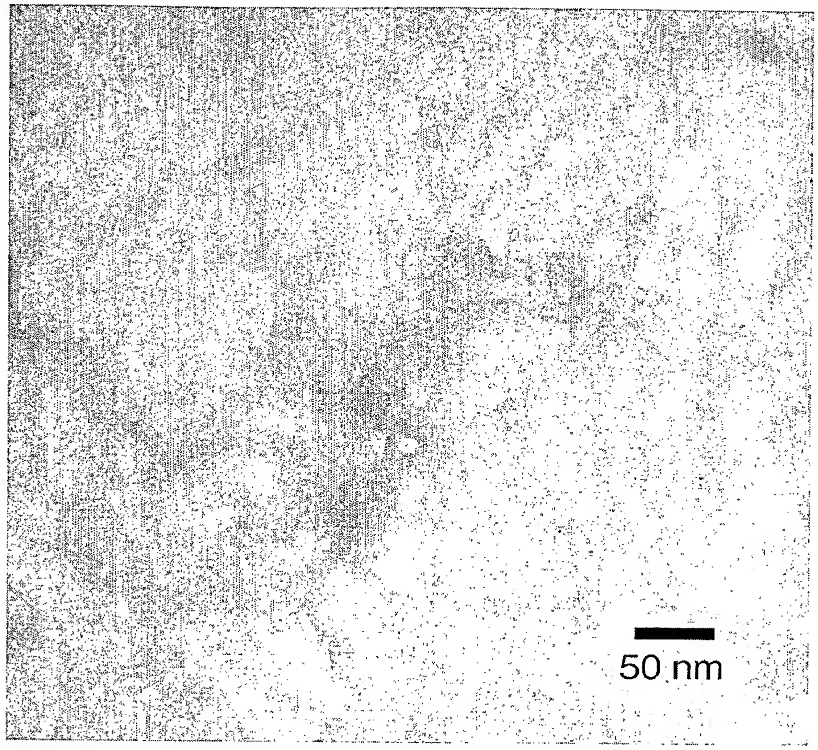


FIGURE 9

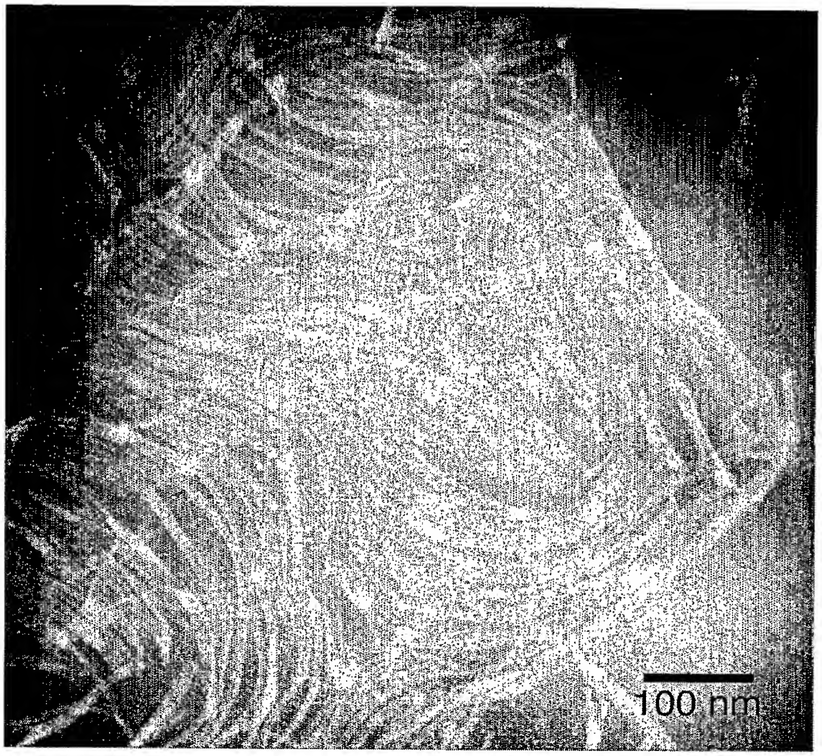


FIGURE 10

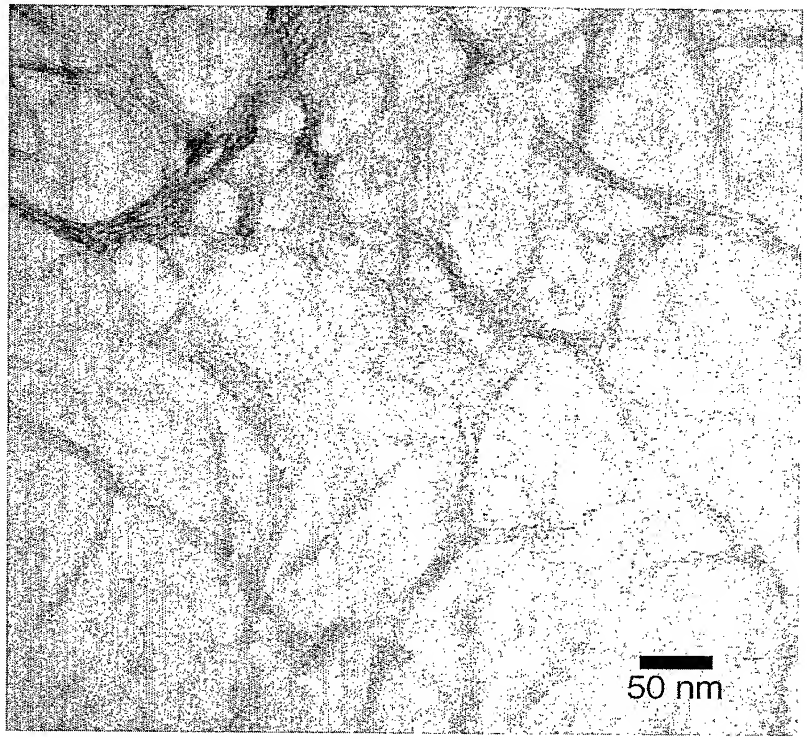


FIGURE 11

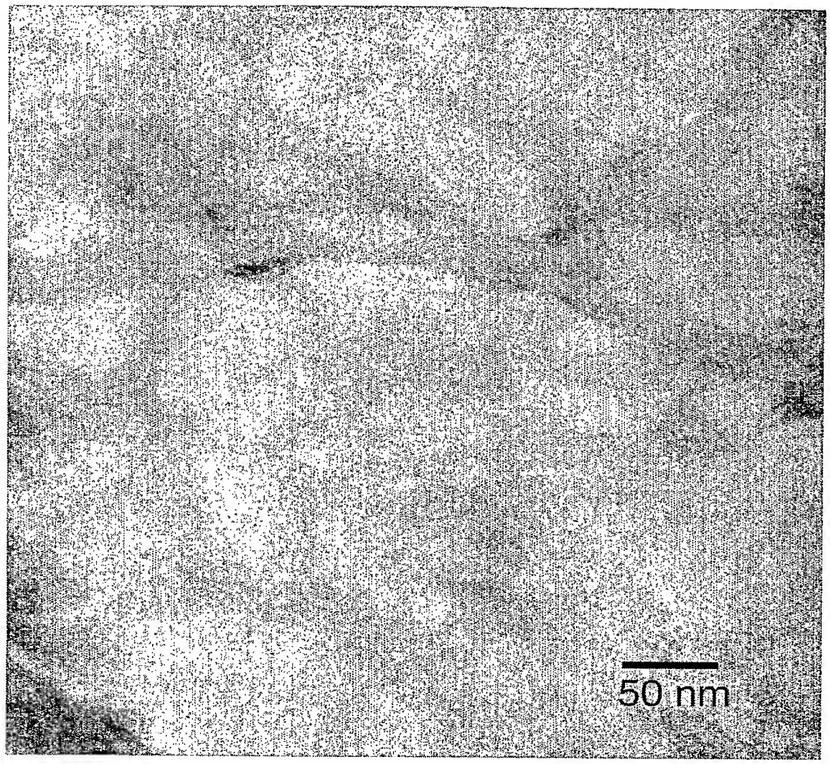


FIGURE 12

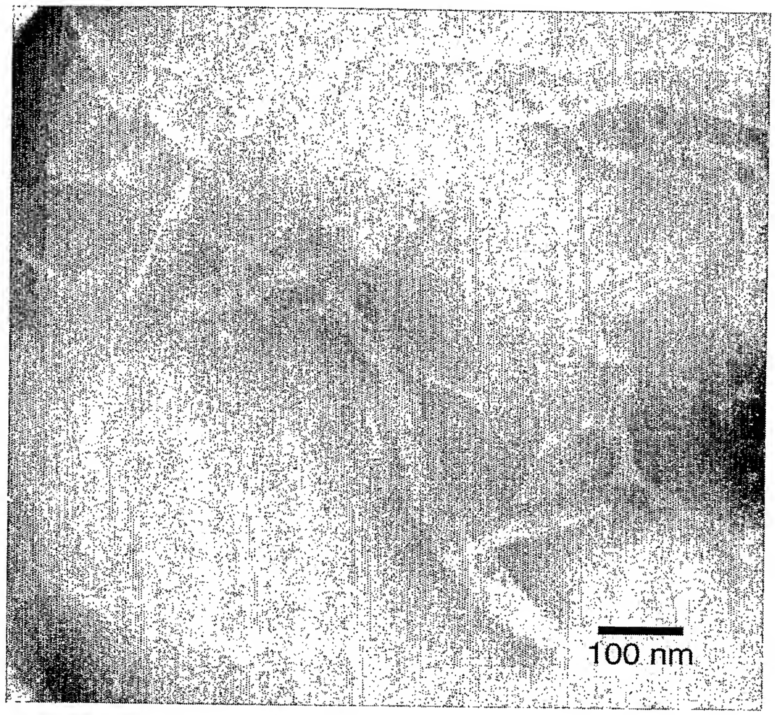


FIGURE 13

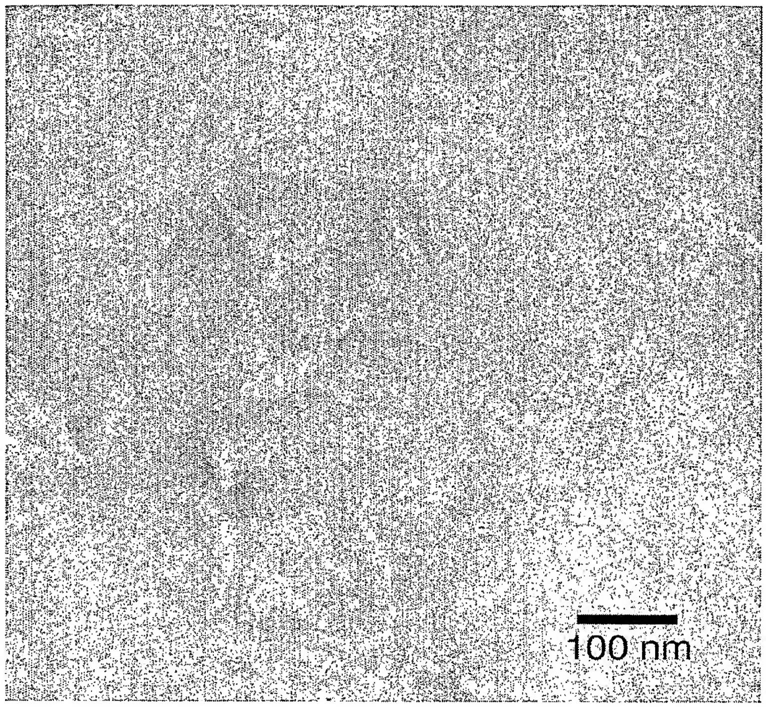


FIGURE 14